HISTORY OF ASPARTAME

Modified and Additional Material by Arthur M. Evangelista, a former FDA Investigator
Original Authors of the Two Main Components: Alex Constantine and Gregory Gordon
Web Site: http://www.qualityassurance.synthasite.com

Posted: 12 March 2004

1964

The development of new pharmaceuticals was the focus of research at the international pharmaceutical company, G.D. Searle and Company (Farber 1989, page 29). A group working on an ulcer drug was formed including Dr. Robert Mazer, James Schlatter, Arthur Goldkemp and Imperial Chemical. In particular, they were looking for an inhibitor of the gastrointestinal secretory hormone gastrin (Stegink 1984a).

1965

In 1965, while creating a bioassay, an intermediate chemical was synthesized -- aspartylphenylalanine-methyl-ester (aspartame). In December of 1965, while James Schlatter was recrystalling aspartame from ethanol, the mixture spilled onto the outside of the flask. Some of the powder got onto his fingers. Later, when he licked his fingers to pick up a piece of paper, he noticed a very strong sweet taste. He realized that the sweet taste might have been the aspartame. So, believing that the dipeptide aspartame was not likely to be toxic, he tasted a little bit and discovered its sweet taste (Stegink 1984a, page 4). The discovery was reported in 1966, but there was no mention of the sweetness (Furia 1972).

1969

The investigators first reported the discovery of the artificial sweetener in the Journal of the American Chemical Society stating (Mazur 1969):

> "We wish to report another accidental discovery of an organic compound with a profound sucrose (table sugar) like taste . . . Preliminary tasting showed this compound to have a potency of 100-200 times sucrose depending on concentration and on what other flavors are present and to be devoid of unpleasant aftertaste."

Today, hundreds of millions of Americans, and millions more world-wide, consume foods and soft drinks stamped with the NutraSweet "swirl", dump packets of Equal in their coffee, and consume NutraSweet-flavored cereal, puddings, gelatins, cheesecake, chewing gum, diet soft drinks, children's vitamins, chilled juices, and 9,000 other products.

So, what is aspartame, a.k.a. NutraSweet, Spoonful, Equal...etc.? aspartyl phenylalanine-methyl ester.

Aspartame ($C_{14}H_{18}N_2O_5$) is a compound of three components. These components are methanol, aspartic acid and phenylalanine (the latter being free form amino acids).

Methanol (methyl alcohol or wood alcohol) is a colorless, poisonous, and flammable liquid. It is used for making formaldehyde, acetic acid, methyl t-butyl ether (a gasoline additive), paint strippers, carburetor cleaners for your car's engine, and chloromethanes, et al. This poison can be inhaled from vapors, absorbed through the skin, and ingested.

Methanol is the type of alcohol you read about when people become blind from drinking it. In aspartame, methanol poisoning and poisoning from methanol's breakdown components (formaldehyde and formic acid) can have widespread and devastating effects. This occurs in even small amounts, and is especially damaging when introduced with toxic, free-form amino acids, called excitotoxins.

Methanol is quickly absorbed through the stomach and small intestine mucosa. The methanol is converted into formaldehyde (a known carcinogen). Then, via aldehyde hydrogenase, the formaldehyde is converted to formic acid. These two metabolites of methanol are toxic and cumulative.

Phenylalanine is an amino acid. Well, amino acids are good for us, right? Don't they keep us healthy? The answer is yes, amino acids are necessary for good health, EXCEPT when you separate the individual amino acid from its protein chain, and use it as an "isolate" or by itself.

The Aspartic acid, in aspartame, is also an excitotoxin. An excitotoxin, is a deleterious substance that excites or over-stimulates nerve cells. This occurs in the brain, as well as the peripheral nerves, because aspartic acid, in free form, is an absorption accelerant & easily crosses the blood-brain barrier.

This pathological excitation of nerve cells creates a breakdown of nerve function, as we will see. Basically, they are a group of compounds that can cause special neurons within the nervous system to become overexcited to the point that these cells will die.

That's right, they are excited to death. Excitotoxins include such things as monosodium glutamate (MSG), aspartate, (a main ingredient in NutraSweet), L-cysteine (found in hydrolyzed vegetable protein) and related compounds.

What makes this all the more intriguing is that "excitotoxins" appear to play a key role in degenerative nervous system diseases such as Parkinson's disease, Alzheimer's disease, Huntington's, ALS (Lou Gehrig's disease) and many others.

But the story doesn't stop there. It appears that an imbalance of these excitotoxins during critical periods of brain development can result in an abnormal formation of brain pathways; that is, a "miswiring of the brain." This may lead to serious disorders such as behavioral problems (hyperactivity, aggression, attention deficit disorders, learning disorders, poor learning ability, and ADD)-and a lifetime of endocrine problems such as menstrual difficulties, infertility, and premature puberty.

One of the earliest observations seen in animals exposed to large doses was gross obesity. Some neuroscienttists have voiced concern that America's explosion of childhood obesity may be related to excitotoxins in food.

Aspartame creates altered brain function, nerve damage, and systemic organ complications. Information collected reveals that aspartame clinically exacerbates any borderline (even yet undetected) predisposing illness, and absolutely complicates certain known medical illnesses like Lupus, Multiple Sclerosis, Parkinson's, diabetes, retinopathies, allergies, mentation disorders, etc. (See list of symptoms 1)

Aspartame is a toxin, and is unique in this hazardous respect. This in NOT an allergic reaction, but rather a true toxin. No other food can be provided as a comparison to the toxic nature of NutraSweet. Upon closer examination, the available research revealed that the manufacturer (Monsanto) and the FDA are manipulating the public (via the media) into thinking that aspartame is safe. It is not. As an American who trusted the system we all created, as an American who worked for the system, it made me angry that public health has taken a backseat to greed. This is the "engine" that perpetuated this epidemic: the collusion of our government with multi-national conglomerate influence.

G.D. Searle approached Dr. Harry Waisman, Biochemist, Professor of Pediatrics, Director of the University of Wisconsin's Joseph P. Kennedy Jr. Memorial Laboratory of Mental Retardation Research and a respected expert in phenylalanine toxicity, to conduct a study of the effects of aspartame on primates. The study was initiated on January 15, 1970 and was terminated on or about April 25, 1971. Dr. Waisman died unexpectedly in March, 1971.

Seven infant monkeys were given aspartame with milk. One died after 300 days. Five others (out of seven total) had grad mal seizures. The actual results were hidden from the FDA when G.D. Searle submitted its initial applications.

G.D. Searle denied knowledge of or involvement with the initiation, design or performance of the study. Yet, false results were submitted to the FDA like the rest of the 150 G.D. Searle studies (on aspartame and other products), bearing a Searle Pathology-Toxicology project number. Both Dr. Waisman and G.D. Searle were responsible for the study design. A number of false statements were made by G.D. Searle including that the animals were unavailable for purchase for autopsy after the termination of the study.

The FDA banned the sweetener cyclamate, 1969. Robert Scheuplein, who was the acting Director of FDA's Toxicological Services Center for Food Safety and Applied Nutrition was quoted as saying "the decision was more a matter of politics than science."

Neuroscientist and researcher John W. Olney found that oral intake of glutamate, aspartate and cysteine, all excitotoxic amino acids, cause brain damage in mice (Olney 1970). Dr. John W. Olney informed G.D. Searle that aspartic acid caused holes in the brains of mice.

Ann Reynolds, a researcher who was hired by G.D. Searle and who has done research for the Glutamate (MSG) Association, and was asked to confirm Dr. Olney's tests. Dr. Reynolds confirmed aspartame's neurotoxicity in infant mice.

Excitotoxic compounds like MSG, aspartate, cysteine seem to create hypothalamic lesions, particularly in young animals. The reason for the latter is likely the fact that the blood brain barrier closes most slowly (if ever completely) around structures like hypothalamus. The outcome for such animals (rats) was obesity,severe behavioral changes, etc.

G.D. Searle did not inform the FDA of this study until after aspartame's approval. None of the tests submitted by G.D. Searle to the FDA contradicted these findings (Olney 1970, Gordon 1987, page 493 of US Senate 1987).

An internal G.D. Searle memo laid out the strategy for getting aspartame approved (Helling 1970):

> At this meeting [with FDA officials], the basic philosophy of our approach to food and drugs should be to try to get them to say, "Yes," to rank the things that we are going to ask for so we are putting first those questions we would like to get a "yes" to, even if we have to throw some in that have no significance to us, other than putting them in a yes saying habit.
> We must create affirmative atmosphere in our dealing with them. It would help if we can get them or get their people involved to do us any such favors. This would also help bring them into subconscious spirit of participation.
> (Refer to Actual Letter...2)

1972

FDA Toxicologist Dr. Adrian Gross came upon some irregularities in the submitted tests of the G.D. Searle drug Flagyl. G.D. Searle did not respond for another two years. Their response raised serious questions about the validity of their tests (Gross 1975, page 35)

1973

On March 5, 1973, G.D. Searle's petition to the FDA for approval to market aspartame as a sweetening agent was published in the Federal Register (1973).

On March 21, 1973 the MBR report was submitted to G.D. Searle. Background: In August of 1970, G.D. Searle conducted two 78- week toxicity studies on rats for what was to become a best-selling heart medication, Aldactone. One study was conducted at G.D. Searle and one at Hazelton Laboratories.

In March 1972, the rats for autopsied and the pathology slides were analyzed. For confirmation of the results, G.D. Searle sent the slides to Biological Research, Ltd. where board certified pathologist, Dr. Jacqueline Mauro examined the data. She discovered that the drug appeared to induce tumors in the liver, testes, and thyroid of the rats. The report submitted to G.D. Searle by Dr. Mauro was known as the MBR Report.

These statistically significant findings were confirmed by G.D. Searle's Mathematics- Statistics Department.

Instead of submitting these alarming findings to the FDA, G.D. Searle contracted with another pathologist, Dr. Donald A. Willigan.

He was given 1,000 slides to examine. The Willigan Report was more to G.D. Searle's liking because it revealed a statistically significant increase in thyroid and testes tumors, but not in liver tumors. Liver tumors are of much more concern to the FDA. The Willigan Report was immediately submitted to the FDA. G.D. Searle did not disclose the MBR Report to the FDA until August 18, 1975, 27 months after it had been given to G.D. Searle.

At first, G.D. Searle claimed that they did not submit the MBR Report to the FDA because of an "oversight."

The FDA Commissioner from 1972 to 1976, Alexander Schmidt, M.D. felt that "Superficially, it seemed like, if there would ever be a safe kind of product, that would be it. The idea that two naturally-occurring amino acids could harm someone in relatively small amounts...."

In an FDA memorandum dated September 12, 1973, Martha M. Freeman, M.D. of the FDA Division of Metabolic and Endocrine Drug Products addressed the adequacy of the information submitted by G.D. Searle in their petition to approve aspartame (Freeman 1973):

> "Although it was stated that studies were also performed with diketopiperazine [DKP] an impurity which results from acid hydrolysis of Aspartame, no data are provided on this product."

Commenting on one particular single dose study:

> "It is not feasible to extrapolate results of such single dose testing to the likely condition of use of Aspartame as an artificial sweetener."

It is important to note that Dr. Freeman pointed out the inadequacy of single-dose tests of aspartame as early as 1973.

Matalon said, "Let us say cigarettes were invented today, and you give 20 people two packs a day and after six weeks, no one has cancer, would you safe that it was safe? That's what they did with NutraSweet."

Since then, the NutraSweet Company has flooded the scientific community with single-dose studies.

"Chemistry - No information is provided other than formulae for Aspartame and its diketo-piperazine."

Pharmacology - Reference is made to 2 year rat studies, but no data are provided on acute or chronic toxicity."

"Clinical - No protocols or curriculum vitae information are provided for the 10 completed clinical studies. Results are reported in narrative summary form, and tabulations of mean average values only.

No information is given as to the identity of the reporting labs, methodology (except rarely), or normal values. (Reported units for several parameters cannot be verified at this time.)

"No pharmacokinetic data are provided on absorption, excretion, metabolism, half-life; nor bioavailability of capsule vs. food-additive administration."

Dr. Freeman concludes:

> "1. The administration of Aspartame, as reported in these studies at high dosage levels for prolonged periods, constitutes clinical investigational use of a new drug substance."
> "2. The information submitted for our review is inadequate to permit a scientific evaluation of clinical safety."

She went on to recommend that marketing of aspartame be contingent upon proven clinical safety of aspartame. The FDA Bureau of Foods rejected Dr. Freeman's recommendation.
(Congressional Record 1985a)

Construction of a large aspartame manufacturing plant in Augusta, Georgia was halted. It was thought that aspartame's uncertain regulatory future was the main reason for the stopping of construction (Farber 1989, page 47). In the 1973 G.D. Searle Annual Report, an executive stated that "commercial quantities of the sweetener will be supplied from the enlarged facility of Ajinomoto."

Ajinomoto is the inventor and main producer of the food additive MSG.

1974

Ninety of the 113 aspartame studies which were submitted by G.D. Searle to the FDA were conducted in the early to mid- 1970's. All of the tests that were described by the FDA as "pivotal" were conducted during this time. Eighty percent of these tests were conducted by G.D. Searle or by their major contractor, Hazleton Laboratories, Inc.
(Graves 1984, page S5497 of Congressional Record 1985a).

Dr. J. Richard Crout, the acting director of the FDA Bureau of Drugs stated that "The information submitted for our review was limited to narrative clinical summaries and tabulated mean values of laboratory studies. No protocols, manufacturing controls information or preclinical data were provided.

Such deficiencies in each area of required information precluded a scientific evaluation of the clinical safety of this product...."

Dr. John Olney and Consumer Interest attorney, James Turner, Esq. met with G.D. Searle to discuss the results of Olney's experiments. G.D. Searle representative's claim that Olney's data raises no health concerns.

On July 26, 1974, just 15 months after Searle petitioned for approval, FDA commissioner Alexander Schmidt approved aspartame use in dry foods, allowing a 30-day period for public hearings and comment. He acted on a strong endorsement from the Bureau of Foods, now called the Center for Food Safety and Applied Nutrition (CFSAN).

It was not approved for baking goods, cooking, or carbonated beverages. This approval came despite the fact that FDA scientists found serious deficiencies in all of the 13 tests related to genetic damage which were submitted by G.D. Searle.

At that point, consumer attorney Turner, author of a 1970 book about food additives, objected to the short comment period.

Turner was joined in his protest by a now-defunct public interest group and by Dr. John Olney, a Washington University neuropathologist who had linked aspartame to brain lesions in mice.

Schmidt promptly froze the approval. In an action that was the first of its kind, he ordered that a Public Board of Inquiry be named to look into aspartame. Schmidt also had been alerted to conflicts between Searle research reports and conclusions from independent animal studies that the firm's anti-infective drug, Flagyl and its cardiovascular drug Aldactone may cause cancer. He named a Bureau of Drugs task force to investigate.

Philip Brodsky, the unit's since-retired lead investigator, said aspartame was included in a broad inquiry into Searle animal studies on five drugs and the Copper-7 intrauterine device to surprise the company. "We didn't think they'd expect us to cover it."

The task force assailed Searle's conduct of research on most of the products, including aspartame, in a searing, 84-page report.

"At the heart of the FDA's regulatory process," the report said, "is its ability to rely upon the integrity of the basic safety data submitted by sponsors of regulated products. Our investigation clearly demonstrates that, in the G.D. Searle Co., we have no basis for such reliance now."

The task force charged, for example, that the company removed tumors from live animals and stored animal tissues in formaldehyde for so long that they deteriorated. Instead of performing autopsies on rhesus monkeys that suffered seizures after being fed aspartame, the company had financed a new monkey study with a different methodology that showed no problems.

For the next seven years, Searle's petition was tied up in reviews by the task force and other sharply critical FDA panels.

At the task force's request, Richard Merrill, the FDA's general counsel, demanded in a letter that Samuel Skinner, the U.S. attorney in Chicago, open a grand jury investigation of Searle and three of its employees.

One Searle official named by Merrill was Robert McConnell, who had been director of Searle's Department of Pathology and Toxicology and oversaw most of the company's aspartame research.

McConnell's Detroit lawyer, Gerald Wahl, said that as the inquiries heated up, his client was suddenly awarded a $15,000 bonus and asked to take a three-year sabbatical by director Wesley Dixon. Wahl said Dixon told McConnell he had become a "political liability," a remark Dixon later denied making.

McConnell received his annual salary of more than $60,000 during the sabbatical at the Massachusetts Institute of Technology, but he never got his job back, and ended up suing the company, Wahl said.

"I've represented hundreds of executives, but I've never seen anybody get the deal that McConnell got," he said. "When you boil it all down, they were looking for continued support from McConnell during the inquiries."

G.D. Searle's responses to queries about the testing of their drug Flagyl, serious and unexpected side effect from other drugs they developed, and information from Dr. John Olney's studies started a controversy within the FDA as to the quality and validity of G.D. Searle's test of aspartame and pharmaceuticals (Congressional Record 1985a).

1975

In July 1975, the FDA Commissioner, Dr. Alexander Schmidt appointed a special Task Force to look at 25 key studies for the drugs Flagyl, Aldactone, Norpace, and the food additive aspartame. Eleven of the pivotal studies examined involved aspartame. All of the studies whether conducted at G.D. Searle or Hazleton Laboratories were the responsibility of the Pathology-Toxicology Department at G.D. Searle. (Gross 1987a, page 430 of US Senate 1987).

The special Task Force was headed by Philip Brodsky, FDA's Lead Investigator and assisted by FDA Toxicologist, Dr. Adrian Gross. The Task Force was especially interested in "pivotal" tests as described in an article from Common Cause Magazine by Florence Graves (Graves 1984, page S5499 of Congressional Record 1985a):

> "Before the task force had completed its investigation in 1976, Searle had submitted the vast majority of the more than 100 tests it ultimately gave the FDA in an effort to get aspartame approved.
> These included all test ever described as 'pivotal' by the FDA. About half the pivotal tests were done at Searle; about one-third were done at Hazleton Laboratories. 'Pivotal' tests include long-term (two-year) tests such as those done to determine whether aspartame might cause cancer.
> Former FDA commissioner Alexander Schmidt said in a recent interview that if a pivotal test is found to be unreliable, it must be repeated 'Some studies are more important than others, and they have to be done impeccably,' Schmidt said."

G.D. Searle executives admitted to "payments to employees of certain foreign governments to obtain sales of their products." (Searle 1975)

Consumer lawyer Turner said, "The notion that an industrial company would take large sums of money and parcel it out to scientific consulting firms and university departments, who they consider to be personal and commercial allies is an unconscionable way to ensure the safety of the American food supply."

He said the NutraSweet experience shows that "the entire system of the way scientific research is done needs to be carefully investigated, evaluated, and revamped."

Food industry officials also said most studies financed by Searle or the NutraSweet Co. have been arranged as contracts, rather than grants. Smith said the company often uses contracts "to accomplish a specific research task."

James Scala, former director of health sciences for the General Foods Corp., a major NutraSweet user, said that a scientist working under contract became "more of an arm of the Searle research group than a grantee."

On July 10, 1975, Senator Edward Kennedy chaired a hearing on drug-related research before the Senate Subcommittee on Health of the Committee on Labor and Public Welfare (US Senate 1975). Preliminary reports of discrepancies discovered about G.D. Searle were discussed.

The findings of the FDA Task Force were later presented at further hearings on January 20, 1976 (US Senate 1976a) and April 8, 1976 (US Senate 1976b).

Chief investigator Brodsky said that "politicized" handling of the task force disclosures, at hearings chaired by Sen. Edward Kennedy D-Mass., was one reason he retired in 1977. He said the main witnesses, Searle executives, and top FDA officials uninvolved in the investigation gave "the wrong answers to the wrong questions"...They didn't even let the experts answer the questions.

On December 5, 1975, Dr. John Olney and James Turner waived their right to a hearing at the suggestion of the FDA General Counsel after the FDA and G.D. Searle agreed to hold a Public Board Of Inquiry (PBOI) (Federal Register 1975).

On December 5, 1975, the FDA put a hold on the approval of aspartame due to the preliminary findings of the FDA Task Force. The Public Board of Inquiry is also put on hold.

The evidence of the aspartame pivotal studies were protected under FDA seal on December 3, 1975 (Sharp 1975).

G.D. Searle had invested 19.7 million dollars in an incomplete production facility and 9.2. million dollars in aspartame inventory. On December 8, 1975, stockholders filed a class action lawsuit alleging that G.D. Searle had concealed information from the public regarding the nature and quality of animal research at G.D. Searle in violation of the Securities and Exchange Act (Farber 1989, page 48).

1976

On January 7, 1976, G.D. Searle submitted to the FDA their proposal for the adoption of "Good Laboratory Practices" (Buzzard 1976b). G.D. Searle's input was used in FDA's adoption of Good Laboratory Practices.

In March 1976, the FDA Task Force completed a 500-page report with 15,000 pages of exhibits (80-page summary) to the FDA after completing their investigation (Schmidt 1976c, page 4 of US Senate 1976b).

A preliminary statement about the breadth of the investigation from FDA Toxicologist and Task Force team member, Dr. Andrian Gross before the US Senate (Gross 1987a, page 1-2):

> "Practices that were noted in connection with any given such study were quite likely to have been noted also for other studies that were audited, and this was a situation which was in no way unexpected: after all, the set of all such studies executed by that firm from about 1968 to the mid- 1970's were conducted in essentially the same facilities, by virtually the same technicians, professional workers and supervisors, and the nature of such studies does not differ much whether a food additive or a drug product is being tested for safety in laboratory animals.
> It is in this sense, therefore, that the overall conclusion summarized at the beginning of the Searle Task Force Report have relevance to all the studies audited in 1975 (whether they had references to aspartame or to any of the six drug products of Searle's) and, by extension, to the totality of experimental studies carried out by that firm around that time -- 1968 to 1975."

A few of the conclusions of the FDA Task Force (Gross 1987a, page 2-3):

> "At the heart of FDA's regulatory process is its ability to rely upon the integrity of the basic safety data submitted by sponsors of regulated products. Our investigation clearly demonstrates that, in the (case of the) GD Searle Company, we have no basis for such reliance now."
> "We have noted that Searle has not submitted all the facts of experiments to FDA, retaining unto itself the unpermitted option of filtering, interpreting, and not submitting information which we would consider material to the safety evaluation of the product . . . Finally, we have found instances of irrelevant or unproductive animal research where experiments have been poorly conceived, carelessly executed, or inaccurately analyzed or reported."
> "Some of our findings suggest an attitude of disregard for FDA's mission of protection of the public health by selectively reporting the results of studies in a manner which allay the concerns of questions of an FDA reviewer."
> "Unreliability in Searle's animal research does not imply, however, that its animal studies have provided no useful information on the safety of its products. Poorly controlled experiments containing random errors blur the differences between treated and control animals and increase the difficulty of discriminating between the two populations to detect a product induced effect.
> A positive finding of toxicity in the test animals in a poorly controlled study provides a reasonable lower bound on the true toxicity of the substance.
> The agency must be free to conclude that the results from such a study, while admittedly imprecise as to incidence or severity of the untoward effect, cannot be overlooked in arriving at a decision concerning the toxic potential of the product."

A few of the relevant findings summarized from various documents describing the FDA Task Force Report:

1. "Excising masses (tumors) from live animals, in some cases without histologic examination of the masses, in others without reporting them to the FDA." (Schmidt 1976c, page 4 of US Senate 1976b) Searle's representatives, when caught and questioned about these actions, stated that "these masses were in the head and neck areas and prevented the animals from feeding." (Buzzard 1976a)

"Failure to report to the FDA all internal tumors present in the experimental rats, e.g., polyps in the uterus, ovary neoplasms as well as other lesions." (Gross 1987a, page 8).

2. G.D. Searle "stored animal tissues in formaldehyde for so long that they deteriorated." (Gordon 1987, page 496 of US Senate 1987; US Schmidt 1976c, page 25, 27 of US Senate 1976b)
3. "Instead of performing autopsies on rhesus monkeys that suffered seizures after being fed aspartame, the company had financed a new monkey seizure study with a different methodology that showed no problems." (Gordon 1987, page 496 of US Senate 1987)
4. "Reporting animals as unavailable for necropsy when, in fact, records indicate that the animals were available but Searle choose not to purchase them." (Schmidt 1976c, page 5 of US Senate 1976b)
5. Animals which had died were sometimes recorded as being alive and vice versa. "These include approximately 20 instances of animals reported as dead and then reported as having vital signs normal again at subsequent observation periods." (Gross 1985, page S10835)
6. "Selecting statistical procedures which used a total number of animals as the denominator when only a portion of the animals were examined, thus reducing the significance of adverse effects." (Schmidt 1976c, page 4 of US Senate 1976b)
7. G.D. Searle told the FDA that 12 lots of DKP were manufactured and tested in one study, yet only seven batches were actually made. (Gross 1985, page S10835)
8. "Significant deviations from the protocols of several studies were noted which may have compromised the value of these studies . . . In at least one study, the Aspartame 52 weeks monkey study, the protocol was written after the study had been initiated." (Gross 1985, page S10835)
9. "It is significant to note that the Searle employee responsible for reviewing most of the reproduction studies had only one year of prior experience, working on population dynamics of cotton tail rabbits while employed by Illinois Wildlife Service. In order to prepare him for this title of 'Senior Research Assistant in Teratology' (fetal damage) Searle bought him books to read on the subject and also sent him to a meeting of the Teratology Society. This qualified him to submit 18 of the initial tests to the FDA, in addition to training an assistant and 2 technicians. He certainly must have kept them busy because Searle claimed that 329 teratology examinations were conducted in just 2 days. He estimated that he himself examined about 30 fetuses a day, but officials for the Center for Food and Applied Nutrition could never determine how that was possible."
10. "In each study investigated, poor practices, inaccuracies, and discrepancies were noted in the antemortem phases which could compromise the study."
11. "Presenting information to FDA in a manner likely to obscure problems, such as editing the report of a consulting pathologist . . . Reporting one pathology report while failing to submit, or make reference to another usually more adverse pathology report on the same slide." (Schmidt 1976c, page 4-5 of US Senate 1976b)
12. Animals were not removed from the room during the twice per month exterminator sprayings. (Gross 1985, page S10836 of Congressional Record 1985b)
13. Often the substance being tested which was given to the animals was not analyzed or tested for homogeneity. "No records were found to indicate that any treatment mixtures used in the studies were ever tested or assayed for pesticide content . . . Running inventory records for

either treatment mixtures or the test compounds used in treatment mixtures are not maintained."

14. In the Aspartame (DKP) 115 week rat study the written observations of the pathology report was changed by the supervising pathologist, Dr. Rudolph Stejskal even though he was not physically present during the autopsies and could not have verified the observations of the pathologist who did perform the autopsies. The pathologist who did perform some of the autopsies had no formal training for such procedures.
15. "Contrary to protocol, slides were not prepared of this [unusual lesions from the Aspartame (DKP) study) tissue for microscopic examinations . . . ."
16. "In the Aspartame 46 weeks hamster study, blood samples reported in the submission to FDA as 26 week values (for certain specified animals) were found by our investigators as being, in fact, values for different animals which were bled at the 38th week. Many of the animals for which these values were reported (to the FDA) were dead at the 38th week." (Gross 1985, page S10838)

    "It is apparent from the report, that the Appendix portion contains all the individual (animal) values of clinical lab data available from the raw data file. A selected portion of these values appears to have been used in computing group means (which were reported to the FDA). It is not clear what criteria may have been used for selecting a portion of the data or for deleting the others in computing the means (reported to the FDA)." (Gross 1985, page S10838 of Congressional Record 1985b)

17. "Searle technical personnel failed to adhere to protocols, make accurate observations, sign and date records, and accurately administer the product under test and proper lab procedures."
18. [There were] "clerical or arithmetic errors which resulted in reports of fewer tumors."
19. [G.D. Searle] "delayed the reporting of alarming findings." FDA Toxicologist and Task Force member, Dr. Andrian Gross stated:

    "They [G.D. Searle] lied and they didn't submit the real nature of their observations because had they done that it is more than likely that a great number of these studies would have been rejected simply for adequacy. What Searle did, they took great pains to camouflage these shortcomings of the study.

As I say, filter and just present to the FDA what they wished the FDA to know and they did other terrible things for instance animals would develop tumors while they were under study. Well they would remove these tumors from the animals."

FDA Lead Investigator and Task Force Team Leader, Phillip Brodsky described the 1975 FDA Task Force members as some of the most experienced drug investigators. He went on to state that he had never seen anything as bad as G.D. Searle's studies.

The report quoted a letter written to G.D. Searle on July 15, 1975 from its consultant in reproduction and teratology, Dr. Gregory Palmer, in regards to a review of some of G.D. Searle's reproductive studies submitted to the FDA; (as noted in the Congressional record)

"Even following the track you did, it seems to me you have only confounded the issue by a series of studies most of which have severe design deficiencies or obvious lack of expertise in animal management. Because of these twin factors, all the careful and detailed examination of fetuses, all the writing, summarization and resummarization is of little avail because of the shaky foundation."

G.D. Searle officials noted that Dr. Palmer did not look at all of the teratology studies (Searle 1976b, page 21). However, there is no credible evidence that would lead a reasonable person to believe that the studies which were not presented to Dr. Palmer were much better. In fact, the evidence shows that it is very likely that all of the studies were abysmal.

The FDA Commissioner at the time, Alexander Schmidt stated (Graves 1984, page S5497 of Congressional Record 1985a):

"[Searle's studies were] incredibly sloppy science. What we discovered was reprehensible."

Dr. Marvin Legator, professor and director of environmental toxicology at the University of Texas and the pioneer of mutagenicity testing at the FDA from 1962 to 1972 was asked by Common Cause Magazine to review the FDA investigation results of G.D. Searle's tests page (Congressional Record 1985a):

"[All tests were] scientifically irresponsible [and] disgraceful.
I'm just shocked that that kind of sloppy [work] would even be sent to FDA, and that the FDA administrators accepted it. There is no reason why these tests couldn't have been carried out correctly. It's not that we are talking about some great scientific breakthrough in methodology."

Senator Edward Kennedy at the April 8, 1976 hearings before the Senate Subcommittee on Labor and Public Welfare stated (Se. Ted Kennedy 1976):

"The extensive nature of the almost unbelievable range of abuses discovered by the FDA on several major Searle products is profoundly disturbing."
"In all of the studies at Searle which have been examined by the FDA in its investigation, the scope of the material being considered included seven years of observation, from 1968 to date, in 57 studies involving more than 5,700 animals with over 228 million observations and calculations."

However, their deliberate misconduct and "lies" (as put by FDA Investigator, Dr. Adrian Gross) invalidated their experiments for the following reasons:

1. Many of the problems with the studies included horrendous experimental designs, questions regarding dosage given, loss of animal tissue and data, etc., etc., which invalidates entire experiments and causes what they claim to be 4 million observations and calculations per study (average) to become irrelevant.
2. Only the key aspartame studies were looked at. It is almost a certainty that the non-key aspartame studies were equally flawed. Therefore, this would invalidate the "hundreds of millions" of observations and calculations made during these studies.
3. The difference between a study showing no statistical difference and a significant statistical difference is often only a few observations or calculations. Therefore, had the myriad of other serious experimental errors not occurred (as detailed above), the observation and calculation mistakes in each experiment investigated would, by themselves, invalidate most of the key studies.

4. It is highly unlikely that the FDA Investigative teams found all of the problems with G.D. Searle's studies. G.D. Searle seemed so intent on covering up their misconduct, that it is quite likely that they were able to hide many of the problems from the FDA.

A series of poorly conceived, flawed studies funded by G.D. Searle were published in Volume 2 (1976) of the Journal of Toxicology and Environmental Health. An Associate Editor of this scientific journal was Robert G. McConnell, the Director of G.D. Searle's Department of Pathology and Toxicology (the department responsible for monitoring the quality of G.D. Searle's pre-approval tests investigated by the 1975 FDA Task Force). Mr. McConnell's story continues later in 1977.

Another G.D. Searle employee, Carl R. Mackerer was an editor of the journal. Another editor of the journal was Thomas R. Tephly, the person responsible for conducting a series of badly flawed blood methanol and formate measurements in NutraSweet-funded studies over the last 15 years.

In July 1976, the FDA decided to investigate 15 key aspartame studies submitted by G.D. Searle in which the 1975 FDA Task Force discovered problems. Three (3) of the studies were investigated at the FDA (E5, E77/78, E89) by a 5-member Task Force headed by FDA veteran Inspector, Jerome Bressler.

On August 4, 1976, G.D. Searle representatives met with the FDA and convinced them to allow G.D. Searle to hire a private agency, University Associated for Education in Pathology (UAREP), and pay them $500,000 to "validate" the other 12 studies.

According the FDA Commissioner during the early 1980s, Arthur Hull Hayes, the UAREP investigation was to "make sure that the studies were actually conducted."

As described by Florence Graves:

> "The pathologists were specifically told that they were not to make a judgment about aspartame's safety or to look at the designs of the tests. Why did the FDA choose to have pathologists conduct an investigation when even some FDA officials acknowledged at the time that UAREP had a limited task which would only partially shed light on the validity of Searle's testing? The answer is not clear.
> "Dr. Kenneth Endicott, Director of UAREP, said in an interview that the FDA had 'reasons to suspect' that Searle's tests 'were not entirely honest.' Because the FDA 'had doubts about [Searle's] veracity,' Edicott said, officials wanted UAREP 'to determine whether the reports were accurate.'
> "FDA scientist Dr. Adrian Gross, in a letter to an FDA official, said, 'speaking as a pathologist, it seemed questionable that the group could do the kind of comprehensive investigation that was required. He pointed in particular to a variety of issues that needed to be investigated. He said some of these would involved closely questioning administrators and lab technicians about their practices. Since many important issues that should be investigated 'have nothing to do with pathology,' he said, only trained FDA investigators were qualified to do a comprehensive evaluation of the testing. . . .
> (SEE LETTER BY DR. ADRIAN GROSS 3)

> "Meanwhile, an interview with Endicott indicates that Adrian Gross was right: the pathologists couldn't--and didn't--carry out a comprehensive review. . . . As former FDA Commissioner Alexander Schmidt put it in a recent interview, UAREP looked at the slides to determine whether they had been misrepresented, but didn't look at the conduct of the experiments in depth. The 1975 [FDA] task force investigation looked at the conduct of the experiments in depth, but did not look at the slides. . . . Endicott agreed . . . 'We could only look at what was there--the tissues.'

The findings of this investigation where released in the Bessler Report in August 1977 (see below).

1977 OUR POLITICAL PROCESS AT WORK:

Donald Rumsfeld, who was a former member of the U.S. Congress and the Chief of Staff in the Gerald Ford Administration, was hired as G.D. Searle's President. Attorney James Turner, Esq. alleged that G.D. Searle hired Rumsfeld to handle the aspartame approval difficulties as a "legal problem rather than a scientific problem." (US Senate 1987).

Rumsfeld hired: John Robson as Executive Vice President. He was a former lawyer with Sidley and Austin, Searle's Law Firm and also served as chairman of the Civil Aeronautics Board, which was then connect to the Department of Transportation.

Robert Shapiro as General Counsel. He is now head of Searle's NutraSweet Division. He had been Robson's Special Assistant at the Department of Transportation.

William Greener, Jr., as Chief Spokesman. He was a former spokesman in the [Gerald] Ford White House.

Donald Rumsfeld is now on the Board of Directors of the Chicago Tribune which recently wrote a glowing article about the NutraSweet Company.

On January 10, 1977, FDA Chief Counsel Richard Merrill recommended to U.S. Attorney Sam Skinner in a 33-page letter detailing violations of the law that a grand jury be set up to investigate G.D. Searle. In the letter, Merrill stated:

> "We request that your office convene a Grand Jury investigation into apparent violations of the Federal Food, Drug, and Cosmetic Act, 21 U.S..C. 331(e), and the False Reports to the Government Act, 18 U.S.C. 1001, by G.D. Searle and Company and three of its responsible officers for their willful and knowing failure to make reports to the Food and Drug Administration required by the Act, 21 U.S.C. 355(i), and for concealing material facts and making false statements in reports of animal studies conducted to establish the safety of the drug Aldactone and the food additive Aspartame."

BRESSLER:

All of the G.D. Searle studies were abysmal as discussed earlier. However, there were two studies where the violations of the law appeared to be especially flagrant. The two studies cited by Merrill were the 52-week toxicity study on infant monkeys performed by Dr. Waisman which G.D. Searle withheld key information from the FDA and the 46-week toxicity study of hamsters where G.D.

Searle had taken blood from healthy animals at the 26th week and claimed that the tests had actually been performed at the 38th week.

Many of the animals from which G.D. Searle claimed had blood drawn from were actually dead at the 38th week. See earlier discussion for references.

On January 26, 1977, G.D. Searle's law firm, Sidley & Austin, requested a meeting with U.S. Attorney Samuel Skinner before a grand jury is convened. One representative of Sidley & Austin at that meeting was Newton Minow who is currently on the Board of Directors at the Chicago Tribune.

On March 8, 1977, in a confidential memo to aides, while he was supposed to be pushing for fraud indictments against G.D. Searle, U.S. Attorney Samuel Skinner stated that he had begun preliminary employment discussions with G.D. Searle's law firm Sidley & Austin. page 497 of US Senate 1987;

On April 13, 1977, a U.S. Justice Department memo urged U.S. Attorney Samuel Skinner to proceed with grand jury investigations of G.D. Searle. The memo points out that the Statute of limitations on prosecution would run out shortly (October 10, 1977 for the Waisman monkey study and December 8, 1977 for the hamster study.

Samual Skinner withdrew from the G.D. Searle case and Assistant U.S. Attorney William Conlon was then assigned to the Grand Jury investigation (Gordon 1987, page 497 of US Senate 1987).

On July 1, 1977, U.S. Attorney Samuel Skinner left his job to work for the G.D. Searle law firm Sidley & Austin. Thomas Sullivan was appointed as Samuel Skinner's successor page 497 of US Senate 1987).

Meanwhile, Much like the earlier team, the five-member FDA task force, headed by veteran Chicago inspector Jerome Bressler, assailed the quality of animal tests into whether the substance might cause birth defects and tumors. The report said Searle laboratory employee Raymond Schroeder, who worked on related research, first told investigators the feed in the study of the aspartame breakdown product DKP (diketopiperazine) was so inadequately mixed it appeared the rats could "discriminate" and avoid eating the DKP. Schroeder, who has worked for another company since 1975, later backed off his statement. He told UPI, "I just didn't feel qualified to speak on something I didn't work on...There's no one twisting my arm."

In August 1977, the Bressler Report pertaining to three key aspartame studies, E5, E77/78 and E89, was released. Some of the findings from the three studies reviewed by the Bressler- led FDA Task Force include.

1. In one study, 98 of the 196 animals died but were not autopsied until as much as one year later. Because of the delay, much of the animal tissue could not be used and at least 20 animals had to be excluded from postmortem examinations.
2. The original pathology sheets and the pathology sheets submitted to the FDA showed differences for 30 animals.

3. One animal was reported alive at week 88, dead from week 92 through week 104, alive at week 108, and finally dead at week 112.
4. An outbreak of an infectious disease was not reported to the FDA.
5. Tissue from some animals were noted to be unavailable for analysis on the pathology sheets, yet results from an analysis of this "unavailable" tissue was submitted to the FDA.
6. There was evidence that the diet mix was not homogeneous allowing the animals to eat around the test substance. This evidence included a picture and statements by a lab technician.
7. Fifteen fetuses from animals in one experiment were missing.
8. Sections from the animals were too thick for examination.
9. There was no documentation on the age or source of the test animals.
10. There was no protocol until one of the studies was well underway.
11. Animals were not permanently tagged to prevent mix-ups.
12. Some laboratory methods were changed during the study, but not documented.

A G.D. Searle pathologist referring to the DKP study was quoted by investigators as saying:

> "You should have seen things when this study was run -- there were five studies being run at one time -- things were a mess!"

The leader of the Task Force, Jerome Bressler, was quoted as saying:

> "The question you have got to ask yourself is: Because of the importance of this study, why wasn't greater care taken? The study is highly questionable because of our findings. Why didn't Searle, with their scientists, closely evaluate this, knowing fully well that the whole society, from the youngest to the elderly, from the sick to the unsick . . . will have access to this product."

Howard Roberts, acting director of FDA's Bureau of Foods, appointed a five-person task force to review the Bressler team's findings pending a decision on whether to throw out the three tumor and birth-defect studies.

Jacqueline Verrett, a senior FDA scientist on the review team, said members were barred from stating opinions about the research quality. "It was pretty obvious that somewhere along that line they (bureau officials) were working up to a whitewash," she said.

"I seriously thought of just walking off of that task force." Verrett, now a private consultant, said that she and other members wanted to "just come out and say that this whole experiment was a disaster and should be disregarded."

But on September 28, 1977, the panel reported that deviations between Searle's raw data and its FDA submissions were "not of such magnitude as to alter its conclusion."

Verrett said the bureau's intent seemed to be "to tone down what was really found." She noted the bureau felt pressure because safety concerns also had been raised about cyclamate, another alternative for the cancer-linked sugar substitute, saccharin.

In October, 1978, a year after ordering the review that helped get Searle's petition back on track, Robert's (acting Director of Bureau of Foods) quit to become vice president at the National Soft

Drink Association. The NSDA's members later marketed a stream of NutraSweet-flavored diet soft drink products.

Reached at NSDA, Roberts dismissed Verrett's criticism, asserting the task force report "really was of no importance." He said he had no concerns about the appearance of his taking the NSDA job, stressing he does not represent NSDA before the FDA. "I sleep well at night," he said.

For each of the major discrepancies found by the Bressler-led Task Force -- those listed above and many others -- there was a comment in the FDA Bureau of Foods Report minimizing the problem. It seemed that no matter how serious the mistakes were, the FDA Bureau of Foods was determined to accept the studies by G.D. Searle.

The experimental errors as described above were so bad that it proved difficult to minimize all of the major errors in these key studies.

In some cases, the best that the CFSAN could do was to say that "The Task Force could find no evidence that this was a deliberate attempt to influence the study." or "It could not be determined if the results would have been altered...."

The Senior Scientist of the FDA Bureau of Foods Task Force, Jacqueline Verrett had left the FDA. Speaking for the UPI Investigation into Aspartame, she said, 'I seriously thought of just walking off of that task force.' Verrett, now a private consultant, said that she and other members wanted to 'just come out and say that this whole experiment was a disaster and should be disregarded.'

In her testimony before the U.S. Senate, Dr. Verrett stated the following (Verrett 1987):

> "This authentication was hence intended to verify that the submitted data had not been altered; that it reflected the actual outcome of the study, and that it did not change substantially, particularly in a statistical sense, the various parameters from which the conclusion of safety had been derived.
> "Our analysis of the data in this manner revealed that in these three studies, there were really no substantial changes that resulted, although in numerous instances, a definitive answer could not be arrived at because of the basic inadequacies and improper procedures used in the execution of these studies.
> "I would like to emphasize the point that we were specifically instructed not to be concerned with, or to comment upon, the overall validity of the study. This was to be done in a subsequent review, carried out at a higher level. . . . . "It would appear that the safety of aspartame and its breakdown products has still not been satisfactorily determined, since many of the flaws cited in these three studies were also present in all of the other studies submitted by Searle. . . . .
> "Well, they told us in no uncertain terms that we were not to comment on the validity of it. And I hoped, although having been there at that point for 19 years, I should have known better, that there really would be an objective evaluation of this beyond the evaluation that we did.
> "I do not feel that that was done, based on what I have read in the GAO report that I have looked at and so forth. They definitely did not objectively evaluate these studies, and I really think it should have been thrown out from day one.

> "We were looking at a lot of little details and easy parameters in this study, when the foundation of the study, the diet and all of these other things, were worthless. We were talking about the jockey when we should have been talking about the horse, that he had weak legs. It is built on a foundation of sand."

The FDA general counsel wrote a letter to Consumer Attorney, James Turner, Esq. responding to Mr. Turner's concern about the quality and validity of G.D. Searle's experiments. The FDA stated, "The Public Board of Inquiry on aspartame should provide a vehicle for definitive resolution, at least for those studies about which you are most concerned.

As will be discussed later, Dr. John Olney and James Turner, Esq. were not allowed to have the quality and validity of the G.D. Searle studies considered at the Public Board of Inquiry.

1978

On December 13, 1978, UAREP submitted its results of their analysis of 12 of G.D. Searle's aspartame studies. UAREP stated in their report that "no discrepancies in any of the sponsor's reports that were of sufficient magnitude or nature that would compromise that data originally submitted." (Farber 1989, page 33) Remember, the Director of UAREP pointed out in an interview that their pathologists did not conduct a comprehensive review of the studies, they only looked at the animal tissues.

As it turns out, UAREP pathologists who examined the test results were discovered to have missed and withheld negative findings from the FDA. In some cases, they completely missed cancerous brain tumors when analyzing the slides. In addition, some of the slides that were to be examined by UAREP pathologists were missing even though they where supposed to have been kept under "FDA seal." (Olney 1987, page 6-7)

FDA Toxicologist Adrian Gross stated that the UAREP review "may well be interpreted as nothing short of a whitewash." (Farber 1989, page 114). Given that the UAREP review results was so biased in favor of G.D. Searle, one wonders why the FDA would allow a company being investigated for fraud to pay $500,000 and hire an outside entity to "validate" their studies.

Even though the UAREP report was biased, there were numerous instances in that report which demonstrated that G.D. Searle had not submitted even marginally accurate findings to the FDA of their pre-approval aspartame tests. For example, in one study, twelve animals actually had cancerous brain tumors, yet UAREP reported to the FDA that only three animals had such tumors.

1979

In March of 1979, the FDA somehow concluded that G.D. Searle's aspartame studies could be accepted. They decide to convene the Public Board of Inquiry (PBOI) which was agreed to by Dr. John Olney and Attorney James Turner more than four years earlier (Federal Register 1979).

In April of 1979, the FDA outlined the specific questions which were to be addressed by the PBOI. The FDA limited the scope of the PBOI to (Federal Register 1981):

1. Whether the ingestion of aspartame either alone or together with glutamate poses a risk of contributing to mental retardation, brain damage, or undesirable effects on neuroendocrine regulatory systems.
2. Whether the ingestion of aspartame may induce brain neoplasms (tumors) in the rat.
3. Based on answer to the above questions.

   (i) Should aspartame be allowed for use in foods, or, instead should approval of aspartame be withdrawn?

   (ii) If aspartame is allowed for use in foods, i.e., if its approval is not withdrawn, what conditions of use and labeling and label statements should be required, if any?

Dr. John Olney, G.D. Searle, and the FDA's Bureau of Foods were allowed to nominate scientists for the 3-person PBOI panel (Farber 1989, page 34, Federal Register 1981, page 38286).

It is important to note that the scope of the review was very limited in light of all of the various adverse reactions reported to the FDA. The PBOI also disallowed any discussion of the validity of the pre-approval experiments because it accepted the word of certain FDA officials that these experiments had been "validated." Finally, the PBOI was told not to consider aspartame in beverages, only in dry goods.

In June of 1979, the acting FDA Commissioner, Sherwin Gardner selected the 3-person Public Board of Inquiry. The panelists were Peter J. Lampert, M.D., Professor and Chairman, Department of Pathology, University of California (San Diego), Vernon R. Young, Ph.D., University of Nutritional Biochemistry, M.I.T., and Walle Nauta, M.D., Ph.D., Institute Professor, Department of Psychology and Brain Science, M.I.T.

Dr. John Olney strongly objected to the Commissioner's selection of one of the panelists, Dr. Vernon Young, on grounds of conflict of interest and lack of qualifications (Olney 1987, page 3). Dr. Young had written nonaspartame- related articles in collaboration with G.D. Searle scientists (Brannigan 1983, page 196).

In addition, Dr. Olney stated that the question of aspartic acid's neurotoxicity should be looked at by a neuropathologist and that Dr. Young was unqualified since his field was Nutrition and Metabolism. Dr. Olney's objections were overruled by acting FDA Commissioner Sherwin Gardner and the panelists who he objected to was assigned to study the issue of aspartic acid toxicity.

One of the PBOI members, Dr. Walle Nauta stated (Graves 1984, page S5498 of Congressional Record 1985a):

> "It was a shocking story we were told [about Searle's animal testing] but, there was no way we could go after it. We had absolutely no way of knowing who was right. We had to take the FDA's word."

Dr. Nauta stated that he would have "definately" considered other tests and factors if he had known that aspartame was planned for use in soft drinks (Graves 1984, page S5503 of Congressional Record 1985a).

1980

The Public Board Of Inquiry voted unanimously to reject the use of aspartame until additional studies on aspartame's potential to cause brain tumors could be done. The PBOI was particularly concerned about experiment E33/34 where 320 rats received aspartame and a much higher percentage of animals in the aspartame group developed tumors than in the control group (Brannigan 1983, page 196).

In addition, the PBOI was concerned about experiment E70 where 80 rats received aspartame. Both the aspartame group and the control group had an unusually high number of tumors, leading one to suspect that both groups were actually given aspartame (Federal Register 1981).

The PBOI did not believe that aspartic acid presented a neurotoxic hazard. Yet, Dr. Olney pointed out that (Olney 1987, page 3):

> "[Dr. Young had a] lack of qualification" and that he "based his decision on a consideration of [aspartic acid] alone without regard to the real issue, i.e., is it safe to add [aspartic acid] to the large amounts of [glutamic acid/MSG] that are already adulterating the food supply?"

In addition, the "conservative" safety plasma level of aspartic acid used by Dr. Young was the level at which half the animals developed brain damage (Brannigan 1983, page 197).

These errors by Dr. Young throw the question of safety of aspartic acid as part of aspartame into doubt. We will address this issue in more detail in a later section.

1981

On January 21, 1981, the day after Ronald Reagan takes office as U.S. President, G.D. Searle reapplied for the approval of aspartame. G.D. Searle submits several new studies along with their application. It was believed that Reagan would certainly replace Jere Goyan, the FDA Commissioner.

G.D. Searle president, Donald Rumsfeld's connections to the Republican party were also thought to play a part in Searle's decision to reapply for aspartame's approval on the day after Ronald Reagan was inaugurated (Gordon 1987, page 499 of US Senate 1987).

According to a former G.D. Searle salesperson, Patty Wood- Allott, G.D. Searle president, Donald Rumsfeld told his sales force that, if necessary, "he would call in all his markers and that no matter what, he would see to it that aspartame would be approved that year." (Gordon 1987, page 499 of US Senate 1987)

Robert Dormer, a lawyer for the NutraSweet Co., said there was nothing special about the Jan. 21 date or the papers filed that day.

But with Reagan's election, it was virtually assured that a republican-appointed commissioner would replace Goyan and decide the appeal- and Searle had strong GOP connections with Rumsfeld at the helm.

Goyan had set up a five-member "commissioner's team" of scientists with no prior involvement in the issue to review the board's ruling.

In April 1981, Arthur Hull Hayes, Jr. was appointed FDA Commissioner by Ronald Reagan (Graves 1984, page S5502 of Congressional Record 1985a).

On May 18, 1981, three of the scientists in the 5-member panel sent a letter to the panel lawyer, Joseph Levitt discussing their concerns about aspartame.

Those three scientists were Satva Dubey (FDA Chief of Statistical Evaluation Branch), Douglas Park (Staff Science Advisor), and Robert Condon (Veterinary Medicine). Dubey thought that the brain tumor data was so "worrisome" in one study that he could not recommend approval of aspartame (Gordon 1987, page 495 of US Senate 1987).

In another study, Dubey said that key data appeared to have been altered Gordon 1987, page 499 of US Senate 1987).

In his UPI Investigation, Gregory Gordon went on to describe the unusual events that followed (Gordon 1987, page 499 of US Senate 1987):

> "[Douglas] Park said that panel lawyer Joseph Levitt hurried the panel to decide the issue. 'They wanted to have the results yesterday,' he said. 'We really didn't have the time to do the in- depth review we wanted to do.'
> "Park said Levitt met frequently with Hayes and 'was obviously getting the pressure to get a resolution and a decision made.'
> "With three of five scientists on the commissioner's team opposing approval, it was decided to bring in a toxicologist for his opinion on isolated issues [Barry N. Rosloff]. Goyan said if the decision were his, he never would have enlarged the team.
> While the panel did not vote, it ended up split 3-3.
> "Levitt, who normally would have been expected to draft an options paper spelling out scientific evidence on key issues, took an unusual tack. He circulated an approval recommendation and only backed off when Dubey, Park, and Condon objected, team members said. Levitt said he was not directed to draft the approval memo, but did so as a 'tactical' step to break the team's weeks-long impasse by forcing each scientist to state his views. 'It worked, didn't it?' said Levitt, who later was promoted to a post as an executive assistant to the FDA Commissioner."

On July 18, 1981 aspartame was approved for use dry foods by FDA Commissioner Arthur Hull Hayes, Jr. overruling the Public Board of Inquiry and ignoring the law, Section 409(c)(3) of the Food Drug and Cosmetic Act (21 U.S.C. 348), which says that a food additive should not be approved if tests are inconclusive.

In an article in Common Cause Magazine, Florence Graves states that two FDA officials said that Arthur Hull Hayes, Jr. wanted to push aspartame approval through in order to signal reforms of the Reagan Administration.

One team member said that during discussions, Hayes, appeared to be abandoning the agency's traditional standard of "reasonable" proof of safety and looking for "proof of hazard."

Hayes' July 1981 approval decision came in the face of a Searle threat to file a suit challenging the regulatory delays.

His ruling relied in part on a late rat study of brain tumors submitted by Ajinmoto, a Japanese company that manufactures aspartame for Searle. That study, however, tested Wistar rats, a strain that some scientists said is more tumor resistant than the Sprague-Dawley rats used in earlier research.

In his decision, Hayes wrote: "Few compounds have withstood such detailed testing and the repeated close scrutiny and the process through which aspartame has gone should provide the public with confidence of its safety."

Between 1979 and 1982, four more FDA officials who participated in the approval process took jobs linked to the NutraSweet industry: Stuart Pape was the Health and Human Services (HHS) Chief Counsel for Foods; acting FDA commissioner Sherwin Gardner;

Albert Kolbye, who was associate director of the Bureau of Foods for toxicology, and Mike Taylor, an FDA lawyer who represented the bureau before the Board of Inquiry. All four denied any conflict of interest. (Mike Taylor: Deminimus Legislation):

1. Mike Taylor was an FDA lawyer who represented the FDA Bureau of Foods at the PBOI and was part of the team that prevented the quality and validity of G.D. Searle's studies from being considered.
2. Sherwin Gardner was the Deputy FDA Commissioner in 1979. In July, 1974, he had signed the initial approval for aspartame's use in dry foods. (This initial approval was later block by objections from James Turner, Esq. and Dr. John Olney.)

   In December, 1979, Sherwin Gardner became a Vice President of Grocery Manufacturers of America, Inc. (GAO 1986). While Mr. Garden claims that he did not discuss aspartame is his 4 meetings with the FDA within a year of leaving that agency or his 20 meetings with the FDA between 1980 and 1986, the organization he worked for does deal directly with aspartame products. It is unlikely that he would have been rewarded with the job had he called for another delay in approval and proposed that safety tests be conducted independently in order to protect the public.

3. Stuart Pape was the Health and Human Services (HHS) Chief Counsel for Foods from October 1976 to March 1979. He served as special assistant to the FDA Commissioner from March 1979 to December 1979.

   He participated in meetings and discussions on aspartame as well as representing the FDA at the PBOI.

   In December 1979, Mr. Pape was given a job by the law firm of Patton, Boggs, and Blow. This law firm provided counsel to the National Soft Drink Association (NSDA).

   Mr. Pape and Howard R. Roberts of the NSDA (who formerly fought for approval of aspartame at the FDA) met with the FDA twice in 1983 where aspartame was discussed. In

1983, the NSDA inexplicably withdrew their objection to aspartame in diet beverage (GAO 1986).

4. Albert Kolbye was the Associate Director of the FDA Bureau of Foods for toxicology.

1983

In late 1982, Searle petitioned for FDA approval to use the sweetener in diet soft drinks and children's vitamins. On a day when Hayes was away, Novitch approved the petition, increasing the acceptable daily intake level for humans by nearly half, from 34 mg to 50 mg per kilogram of body weight.

Novitch, now in private industry, said he and Hayes had worked together on the matter, but declined to say why he was left to sign the approval.

Just weeks later, Hayes resigned under the cloud of an internal Dept. of Health and Human Services investigation into his acceptance of gratuities from FDA-regulated companies - including free rides aboard jets owned by a major NutraSweet user, the General Foods Corp.

Shortly after being named Dean of the New York Medical school, Hayes also became a consultant to the New York-based public relations firm of Burson-Marsteller, which represents the NutraSweet Co. and several major users.

Hayes' former top spokesman, Wayne Pines, who previously had joined the firm, said he approached Hayes because he thought him "an added value" to clients.

Hayes, now president of the E.M. Pharmaceutical Co. in Hawthorne, N.Y., declined comment for this series of articles. He has in the past denied any impropriety in his consulting role, which sources said paid him more than $1000. per day.

Burson-Marsteller vice president, Buck Buchwald stressed that Hayes was not involved in NutraSweet issues and worked but 10 to 15 days a year.

But a former Burson-Marsteller employee, who requested anonymity, said Hayes was hired precisely because of his decision on NutraSweet and other issues affecting company clients.

Sen. Metzenbaum said it was "at the very least...unbecoming, at the very most, it probably was inappropriate" for Hayes to accept the position.

In July 1986, Anthony Brunetti, a FDA consumer product officer who drafted the 1983 notice approving NutraSweet use in soft drinks, also took an industry job, joining the soft drink association as a science advisor. Brunetti said he cleared the move with the FDA's ethics officer.

"My situation," he said, "is no different than many, many people...that go through the revolving door. It can be made to look like there is some duplicity going on. In terms of my own conscious, I have no problem."

Ron Lorentzen, an FDA toxicologist who was asked by current Bureau of Foods chief Sanford Miller to perform a separate, internal review of the agency's handling of aspartame, described it as a "tortured" story.

But despite the myriad questions and revolving door issues, he asserted the FDA responded to each issue "in a way, perfectly reasonable."

Other questions have arisen over the company and industry's funding of researchers who have invariably supported NutraSweet's safety - with the exception of people with the rare disease phenylketonuria. Independent studies have often raised health concerns.

Dr. Lewis Stegink, a pediatrics professor at the University of Iowa who repeatedly has produced studies, that he says, support aspartame's safety, has received more than $1.3 million dollars in research grants and gifts, including lab equipment, from the (NutraSweet) company since the early 1970's, limited university records show.

Metzenbaum said, "If it is a fact that no questions were raised and more than a million dollars was spent, you have to wonder whether their job was done thoroughly as it should be done."

Stegink's longtime research collaborator, Dr. Jack Filer, serves as executive director of the ILSI (International Life Sciences Institute), the Washington foundation that funds aspartame research.

Filer said he sees no conflict in his dual roles as ILSI's executive director and a company researcher, but declined to disclose his ILSI consulting fees.

He said all the Iowa research money has gone to Stegnik. Filer also said the company (NutraSweet) paid him and Setgnik "$2,000. to $3,000." to edit a book, "Aspartame," about research on the sweetener, and another $1,000. or $1,500. to each of the contributors, including researchers whose studies helped the company win FDA approval. The book states that "the extensive research program carried out to demonstrate aspartame safety may serve as a new standard for the study of food additives."

Filer said he had been "maligned over the years for taking money from corporations," but that the funding source never has influenced his findings.

Dr. David Hunninghake of the University of Minnesota was picked to study aspartame's effect on the liver by former Searle research director Daniel Azarnoff, once Hunninghake's mentor at the University of Kansas, a Hunninghake associate said. He said Searle helped design the study.

Susan Schiffman, named to head a Searle-funded Duke University medical School study into NutraSweet's link to headaches, is a former General Foods and Searle consultant. Her research at Duke, where the medical school has a new Searle Center, has fallen under the office of university vice president William Anylan, a former Searle director. Schiffman said Anylan had no role in Searle's promise to cover all costs of the study, which is expected to cost "hundreds of thousands of dollars." She said she took no salary for her work.

Another industry-backed researcher has been Ann Reynolds, now chancellor of California State University at Long Beach. Dr. John Olney asserted that in a 1971 study, Reynolds confirmed his findings that the sweetener destroyed nerve cells in infant mice, but Searle did not notify the FDA until 1975 or 1976, after the FDA's initial review.

Dr. Daniel Azarnoff, Searle's former science director, and other Searle officials have denied withholding any studies from the government.

Reynolds also co-authored a Searle monkey study that contradicted earlier aspartame research leading to seizures in monkeys. Dr. Olney alleged that Reynolds, who did not return phone calls, and several other company-funded researchers "have a pattern of avoiding" scientific peer review. Industry spokesmen contend that few studies by scientific critics of NutraSweet have undergone peer review. But few such clinical studies have been completed because of a funding shortage.

George Liepa, a nutrition professor at Texas Woman's University said he was required to discuss his findings with Searle before reporting that NutraSweet "is safe" for diabetics on hemodialysis. Dr. David Horwitz, an associate professor of medicine at the University of Illinois, who studied NutraSweet and diabetics, said the company did not influence the outcome, but, "The results were favorable.... Obviously, that is perhaps why Searle was eager to fund an additional study of ours."

Dr. Richard Wurtman was an ardent defender of NutraSweet's safety at public hearings six years ago (1981). Now he is one of the artificial sweetener's harshest critics.

"I think the likelihood is very strong that NutraSweet does produce serious and potentially damaging brain effects in a number of people," the nationally known neuroscientist from Massachusetts Institute of Technology said in a recent series of interviews.

Wurtman's seemingly enigmatic flip-flop from a position as a G.D. Searle Co. consultant to a role as a foe urging restrictions on marketing the firm's best-selling product appears to be much at the center of the controversy over NutraSweet's safety.

Wurtman says his views simply changed with the evolution of his scientific studies and his growing skepticism of industries attitude toward research. His sometimes stormy relationships with the company and an industry-funded foundation, the ILSI, provide a glimpse of the maneuverings surrounding research into a major food additive.

Wurtman, a brash-talking, hard-driving head of a major research laboratory, said he unilaterally severed his consulting relationship with Searle in 1985 after he grew concerned about NutraSweet's effects and the company's inaction. He said he rejected several approaches by the firm, (the NutraSweet Co.) since its sale that year to the Monsanto Corp., to rekindle the consulting arrangement.

Wurtman accuses NutraSweet Co. officials of "misrepresenting" the nature of company-financed studies into links between the sweetener, generically known as aspartame, and epileptic seizures, of sidestepping key safety issues, and of threatening to veto his grant application to ILSI's aspartame committee. A spokesman for the NutraSweet Co. described Wurtman's public attacks as a "political issue," but declined to elaborate.

Wurtman's relationship with Searle, The NutraSweet Co., and many of the companies that sell NutraSweet-flavored products dates to 1978. Beginning that year, according to public records, ILSI provided more than $200,000. to finance his research on caffeine, a common beverage ingredient that was under FDA scrutiny.

Wurtman said he found no ill health effects during his caffeine research, and his relationship was "excellent" with ILSI - a spin-off of the National Soft Drink Association.

During the same period in 1978, he said he rejected a Searle offer of financial support for research on amino acids. Phenylalanine and aspartic acid, two such amino acids, are the main components of NutraSweet.

He said Dr. Sanford Miller, chief of FDA's Bureau of Foods, later sought his testimony before a 1980 Public Board of Inquiry because he openly stated his belief that neither glutamate nor aspartic acid, a similar compound to that in NutraSweet, would not cause brain damage. Wurtman strongly defended aspartame at the hearing.

He said he did not focus on phenylalanine until about 1983, when he learned the FDA was considering expanding use of the low-calorie sweetener, approved two years earlier for dry foods, to include carbonated soft drinks.

From his caffeine research, Wutman said, he was aware of the exploding soft drink market and concluded "that the use of aspartame was going to go up considerably."

"I was genuinely concerned that there might be an increase in brain phenylalanine levels."

Wurtman said that, while phenyalanine is vital to the brain, it can serve as a barrier to 20 other amino acids that provide protein. It is also a well known neurotoxin.

WASHINGTON (UPI) In October 1982, Sen. Howell Heflin, D-Ala, proposed an obscure amendment altering the laws covering U.S. patent extensions, a move affecting only one company and one product, the artificial sweetener, aspartame.

Without mentioning aspartame, which is sold under the name NutraSweet, the senate passed the amendment to the Orphan Drug Act, extending G.D. Searle Co.'s domestic monopoly on aspartame sales for another five years, 10 months, and 17 days.

"We think it's an excellent amendment," remarked Sen. Orrin Hatch, R-Utah, wrapping up a five-minute discussion on the Senate floor.

When the House approved the same language a month later, it all but cinched another $3.5 billion to $4 billion in revenues for the Chicago-based, Searle. It helped Searle's stockholders sell the company's assets, including its lucrative NutraSweet division and the two domestic use patents, for $2.7 billion to the Monsanto Corp. in the summer of 1985.

Sponsors of the measure found their campaign committee, enriched.

Heflin's 1984 reelection committee received contributions totaling at least $9,000. from Searle's top officers and its political action committee, more than any others among a long list of Searle beneficiaries in Congress, federal Election Committee records show.

Hatch's committee received at least $3,000 the records show. Heflin defended his sponsorship of the measure, saying Searle had been victimized by regulatory delays that ate up most of its 17-year patent. But a spokesman for the U.S. Patent Office said Heflin's legislation marked one of only a handful of instances in the last three decades in which a company's patent has been extended by a private bill in Congress.

It also provided a glimpse of the adeptness with which Searle, Monsanto, and their lobbyists have guided the artificial sweetener through the obstacles of government regulatory bureaucracies to capture big financial rewards.

Headed by Donald Rumsfeld, the former Ford White House Chief of Staff, Searle repeatedly demonstrated its political acumen on other front, too, in the years prior to the sale to Monsanto.

In 1981, the company overcame a controversy-snarled, eight-year review process to win Food and Drug Administration approval for NutraSweet.

In 1984, Searle parried an assault on the sweetener's safety from Arizona food scientist, Dr. Woodrow Monte, after hiring Arizona Gov. Bruce Babbitt's former chief of staff as a lobbyist. Searle officers passed along campaign contributions of $2,000 to a key lawmaker, and the company soon had won passage of legislation crushing Monte's efforts to force tough state restrictions on the sweetener.

"I don't know of any company that has apparently covered all of its bases as well as has Searle," said Sen. Metzenbaum (D-Ohio). "Whether it has to do with the scientists or lawyers, or non-profit institutions, or universities, or whatever; in every instance, I have found that they have expended their dollars very carefully and very wisely, but without apparent restraint as to the amount."

Indeed, besides Searle's hiring of up to a dozen lobbyists, UPI traced nearly $200,000. in federal campaign contributions between 1973 and 1986 from its officers and political action committee.

The political intervention in the patent process drew the ire of several small companies seeking to enter the aspartame market, triggering charges that a corporate giant benefited from unjustified or preferential treatment. "I think its obvious they (Searle officials) used political muscle," Alan Kligerman, president of Lactaid, Inc., a New Jersey diet food manufacturer, said of the patent extension. He said his firm had been interested in manufacturing aspartame until the patent was extended, but "Searle was well wired in."

"It is possible that they (the Senate) did not know what they were passing," he said. "I don't know how they got that through, except with the right phone calls."

"I would not hesitate to say," Metzenbaum said, "that the manner in which that five-year extension of the patent rights was put through on the floor of the U.S. Senate was totally inappropriate."

"It should not have been without the entire body being advised that, that issue was going to be on the floor of the Senate."

Metzenbaum said that the Senate has an "alert" system under which all legislation is cleared with individual senators before it is brought to the floor, but the system was bypassed.

Jerry Ray, a spokesman for Heflin, asserted the offices of key senators, including Metzenbaum, approved the measure before it went to the floor. But Ray offered no explanation for the failure to fully disclose the contents and impact of the measure.

Ray quoted Heflin, Chairman of the Senate Ethics Committee, is saying Searle representatives never mentioned campaign contributions in asking him to sponsor the amendment.

Heflin said he has "supported all patent restoration bills" because regulatory delays have created "a chronic problem" in which companies get so little use out of their 17-year patents, they are reluctant to put money into research.

Heflin said, in Searle's case, "almost 35 percent of the patent term had been used on a long series of administrative hearings, trials, and appeals (in) which, in the end, the corporation finally prevailed. To not restore some of the patent term lost would unfairly penalize them."

G.D. Searle sought an extension of its patent on grounds that the Food and Drug Administration's handling of its aspartame approval petition was "an unparalleled instance of unnecessary regulatory delay, which worked a great injustice to Searle".

Critics argue that, to the contrary, the FDA suspended its 1974 approval allowing Searle to market the sweetener because of evidence the company's animal studies were flawed and the results were misrepresented to the FDA in the early 1970's.

The evidence prompted FDA chief counsel Richard Merrill to ask the U.S. Attorney's office in Chicago to open a grand jury investigation into possible fraud by the company.

While a grand jury investigated similar allegations related to Searle drug products, no such inquiry was ever begun into the aspartame testing. But the FDA was concerned enough about Searle's research to appoint two task forces, a university research group, and a Public Board of Inquiry to review various studies.

In 1981, shortly after taking office, FDA commissioner Arthur Hull Hayes, Jr. overturned the three-man Board of Inquiry and approved sale of NutraSweet in dry foods. Two years later, Hayes' deputy, Mark Novitch, approved the use of aspartame in soft drinks.

Kligerman dismissed as "crap" Searle's contention it had been victimized by the FDA bureaucracy, which delayed a decision from 1975 to 1981.

"The FDA had reason for doing this," Kligerman said of the intense review process. "It was not an unnecessary delay. It was Searle's fault this happened." For Purification Engineering, Inc. of

Columbia, Md., which raised money from private investors and built a plant solely to manufacture aspartame for Searle, the congressional action ultimately turned out to be devastating.

Searle officials declined to discussed the patent extension, but a company lobbyist, former White House official William Timmons, said the company "felt there was an injustice" in the delays following aspartame's 1974 approval.

He said the company "took an advocacy role by talking to a lot of members of Congress".

In May of 1984, FEC records show Heflin's reelection committee additionally received $1,000 donations each from Daniel Searle, the chief executive officer of the giant pharmaceutical company; his wife, Dain; William Searle, Searle's brother who was a company director; William Searle's wife, Sally; Suzanne Searle Dixon, a sister of the Searles; and her husband, Wesley Dixon, who also was a company director.

Heflin also received $1,000 from William Searle prior to the general election, and $2,000 in Searle PAC contributions, FEC records show.

On November 1982, a week after his reelection and a month after praising the amendment in the Senate chambers, Hatch's committee received $2,000. in contributions from top Searle officers, the records show.

Sen. Robert Byrd (D-W.Va.), who brought the amendment up for a vote on Heflin's behalf, also received a $1,000 campaign contribution from Daniel Searle on Sept. 25, 1981.

Hatch received contributions of $1,000 each from Daniel Searle, Wesley Dixon, and William Searle on Nov. 11, 1982, days after he was reelected to a second term in which he continued as chairman of the Labor and Human Resources Committee that oversees the FDA.

As chairman of the panel until last January, Hatch repeatedly blocked Sen. Metzenbaum's calls for new hearings into the safety of NutraSweet.

Prior to his reelection, Hatch also received $2,500 in contributions from the soft drink PAC.

Rep. Henry Waxman (D-Calif.), who sponsored the Orphan Drug Act covering research for treating rare diseases and who carried Heflin's patent amendment to the bill in the House, received $1,500 in campaign contributions from the soft drink PAC, including $500 two days before the measure's introduction in the House.

Like Heflin, Waxman made no mention of aspartame in describing the Senate amendments to the drug act on the House floor.

Searle also flashed its political prowess after Arizona scientist Woodrow Monte stirred up a furor in 1984 by publicly assailing NutraSweet's safety.

The ensuing events, Monte charged, "reflected exactly what Searle has been doing all along. They've been buying their way into the hearts and minds of America. They've been using their financial acumen to get their way."

Within months, legislative rules were swept aside one day in early 1985 and, in a swift, subtle maneuver without notice to the public, Monte's campaign for state regulations on the sweetener was sidetracked.

Monte was a leading national advocate in the drive to block marketing of NutraSweet until his own credibility was damaged in 1984 with disclosures he had invested in "put options" that would have earned profits if Searle's stock dropped. He now concedes his options trading was a mistake, but denies it influenced his research.

Monte said he was convinced in 1983, when the FDA okayed use of NutraSweet in carbonated beverages, that the sweetener would break down into poisonous quantities of methyl alcohol in diet sodas left in the Southwest sun.

Monte, director of the Food Science and Nutrition Laboratories at Arizona State, and two consumer groups petitioned the Arizona Dept. of Health Services to ban the sweetener.

Monte said his rat studies had shown that chronic ingestion of methyl alcohol causes brain damage similar to that in humans suffering from Multiple Sclerosis, including seizures, amnesia, optic neuritis, numbness, and dizziness. In the desert heat, Monte said, methanol degrades faster into toxic methyl alcohol.

Searle and FDA officials have argued that aspartame contains too little methanol to pose a health hazard.

When Monte and the consumer groups pressed their legal challenge for more than a year, Searle flexed its muscle:

> The company dispatched a coterie of lobbyists to the state capitol, among them Andrew Hurwitz, Gov. Babbitt's former Chief of Staff; prominent Arizona lobbyist Charles Pine; company lawyer Roger Thies, and another company official, David West.

Between August 23, and Sept. 21, 1984 company officers Daniel Searle and his brother-in-law, Wesley Dixon, each contributed $1,000. to the campaign of State House Majority Leader Burton Barr, later a GOP candidate for governor, reports to the Arizona Secretary of State's office records show.

Campaign disclosure forms show revealed that, during the same period, several House Republicans received contributions from the Committee to reelect Barr, including State Reps. Don Aldridge, Karen Mills, and Jan Brewer, all among the Health Committee members who voted 13-0 to pass the measure affecting NutraSweet.

The trio received $1,500, $1,000 and $750 respectively from Barr, who for years has enhanced his influence by donating to colleagues' campaigns. Barr and Arizona State University Regent William Reilly contacted the school's president, J. Russell Nelson, and Academic Vice President Jack

Kinsinger to inquire into Monte's public attacks on NutraSweet, published reports said. Kinsinger insisted that the issue caused no delay in his decision to grant Monte tenure. Barr did not return phone calls.

When Monte's first petition was rejected and he filed for reconsideration, Hurwitz (Searle) wrote a letter offering legal advice to the Dept. of Health Services (DHS) about its response, and sent copies to Barr and aides to Gov. Babbitt.

In April of 1985, about the same time Monte and his associates finally were to be granted a hearing before the state agency on their petition, they learned that the Arizona Legislature had used a rare maneuver to change the law, without public notice to bar state regulation of FDA-approved food additives. The measure passed under the misleading title of a toxic waste bill.

Monte's campaign to ban NutraSweet in Arizona prompted the State Dept. of Health Services to conduct a study to determine how much NutraSweet soft drinks degraded in high-temperature conditions. The study, completed in July 1984, found that methanol levels were highest (9.4 ppm), in Diet 7-Up samples stored the longest time in the warmest temperature, 99^{o} F heat.

Present and former Arizona state officials have told UPI that the study concerned DHS officials enough that they discussed a NutraSweet ban.

But Norman Peterson, manager of the DHS's Office of Chronic Disease and Environmental Health Services, said that the agency concluded that "the FDA address the methyl alcohol question and had all sorts of supporting data. We had no basis for saying that the data they had presented in support was not correct or adequate."

Another source said Peterson was distressed enough that, during a meeting attended by DHS director Donald Mathis, he proposed being allowed to recommend that pregnant woman, and children, limit their consumption of NutraSweet.

Peterson would not confirm the episode, but recalled that he "was upset about the fact that there were so many unanswered questions".

Mathis, who since left the agency, said he was satisfied that it "wouldn't be humanly possible" to ingest levels of NutraSweet that would produce a toxic reaction.

In September 1984, Monte and his associates file suit to force the DHS to impose storage and labeling requirements or ban NutraSweet altogether. But a proposed settlement under which the agency would hold a public hearing was scuttled because it lacked the approval of Mathis' successor, Lloyd Novick. After more negotiations, the DHS agreed to hold a hearing. But before it could take place, the issue was killed by the legislative change.

House Speaker James Sossaman later admitted that the GOP-controlled House violated its own rules in passing a so-called "strike all" amendment. Chairman Bart Baker of the Health Committee engineered the action, in which an existing bill was stripped, replaced with the NutraSweet language and brought to a vote without the required 24 hours public notice.

For Monte, the development was all the more staggering after he had gotten into a jam over his stock purchase. Monte said that, after reviewing files at the FDA and consulting with his lawyer in 1983, he invested less than $2,000 on Searle options, hoping to raise money to support his costly legal battles against the sweetener. He said he ended up losing $1,224.

Lawyer Rick Faerber also invested in part, he said, because of Monte's knowledge of an upcoming CBS story critical of the FDA's approval of aspartame.

He said stock analysts had phoned Monte inquiring about his Arizona petitions and apparently got the idea the developments would depress the stock value. Faerber said he regrets telling Monte that he "didn't think there was anything wrong" with investing, particularly because pro-NutraSweet forces apparently learned of their dealings. CBS employees also bought "put options" but a Securities and Exchange Commission investigation did not lead to any charges.

Shortly after news stories about the investment appeared, Rep. Bob McEwen, (R-Ohio), assailed CBS and Monte for "irresponsible reporting and conflicts of interest" in a brief speech on the floor of the U.S. Senate.

McEwen charged that the "false report" about NutraSweet was aired solely for profit.

But ion his speech, Rep. McEwen did not mention that his top assistant Charles Greener, is the son of William Greener, Jr., Searle's vice president for corporate communications.

Charles Greener who said he was "unaware" of Rep. McEwen's floor speech until after it occurred, said his father never has handled NutraSweet matters and that McEwen did not know any Searle officials.

The success of the Searle family business, founded 80 years ago, is all the more astounding when compared to the company's predicament in 1977 when it plucked Rumsfeld as its president. Facing a company mired in debt, Rumsfeld, a native Chicagoan and former Illinois congressman, quickly hired three other outgoing Ford Administration officials to join him.

As executive vice president, he named John Robson, a former partner in the law firm of Sidley & Austin who had served as President Ford's chairman of the Civil Aeronautics Board. Robert Shapiro, Robson's special assistant at the Transportation Department, was tapped as general counsel. Rumsfeld also hired William Greener, Sr., who had been a spokesman in the Ford White House and Rumsfeld's chief spokesman at the Pentagon.

The pharmaceutical company suddenly was being run by lawyers and politicians. Stomaching a $28 million net loss in his first year, Rumsfeld slashed Searle's operations, selling off more than 30 subsidiaries worth more than $400 million. Before Rumsfeld could mount a full scale effort to lift a FDA freeze on the sale of NutraSweet, Searle was hit with serious new problems.

Suits filed on behalf of 780 women, alleged the company's Copper 7 intrauterine device had caused them to develop pelvic inflammatory disease, an infection of the reproductive tract that can lead to sterility, even death. Before the suits could be settled, Searle sold out to Monsanto.

The huge, St. Louis-based chemical company and its officers were promptly met with stockholder suits alleging they had failed to explore potential safety problems with Searle's biggest moneymakers- Copper 7 IUD and NutraSweet.

Rejecting criticism of the acquisition, Earl Harbison, Jr., executive vice president of Monsanto and Chairman of the Board of its Searle pharmaceutical subsidiary, said in October 1985, that Monsanto "studied this situation (Copper 7 litigation) very closely prior to acquiring Searle, including consultations with independent physicians".

"We satisfied ourselves with the safety and efficacy of the product," he said. Since then, Copper 7 has been pulled off the market. Some lawyers likened the resulting legal morass to the failure of the Dalkon Shield that drove the Richmond-based A.H. Robins Co. into Chapter 11 bankruptcy protection.

But a former Monsanto official, who requested anonymity, said that as part of the sale agreement, Searle set aside reserves to cover the IUD lawsuits. Thanks to NutraSweet, Searle family members Daniel and William Searle and their sister, Suzanne Searle Dixon, to date appear to have walked away unscathed from all the crises and legal battles.

And even if NutraSweet were proved hazardous, the purchase agreement provided "no escrow, reserve or holdback for liability stemming from the potential health hazards attributed to the NutraSweet product line," says one lawsuit filed by Chicago lawyer Robert Holstein on behalf of a Monsanto stockholder.

And Rumsfeld emerged from his nine years with the company in solid financial condition. Securities and Exchange Commission records show that for his guiding the sweeping turnaround, he earned more than $2 million in salaries and more than $1.5 million in bonuses between 1979 and 1984.

"Banana plants don't make NutraSweet," the television announcer noted wryly, and the image of an exotic bird perched in a jungle tree filled the screen. "Neither do cows," said the voice, as the camera cut to a robust-looking heifer wagging its tail. "But they might as well. If you've had bananas and milk, you've eaten what's in NutraSweet."

True, bananas, milk and NutraSweet all contain phenylalanine, one of 21 amino acids that form the "building blocks" of protein. But that doesn't tell the whole story.

Dr. Richard Wurtman, a neuroscientist at the Massachusetts Institute of Technology, says that because NutraSweet lacks other important amino acids normally found in foods, the brain absorbs unusually high levels of phenylalanine that could increase the likelihood of epileptic seizures.

Referring to an ad proclaiming that the body treats the ingredient of the artificial sweetener "no differently than if they came from a peach or a string bean or a glass of milk," Wurtman said, "That's not true."

Dr. Louis Elsas, director of medical genetics at Emory University, groans at the industry arguments that eating or drinking NutraSweet (aspartame) is just like eating a hamburger.

"Phenylalanine is a known toxin to the brain,' Elsas said. "Aspartame is phenylalanine, and drinking aspartame is like drinking phenylalanine as an individual amino acid."

A spokeswoman at the New York offices of Ogilvy and Mather, the lead ad agency on the sweetener account for the Chicago-based NutraSweet Co., declined comment on the allegation. The drumbeat of NutraSweet advertisements has been steady. Beverage Industry, a trade publication, labeled the NutraSweet blitz "probably the largest advertising campaign ever designed around a product ingredient."

Industry sources say that since 1984, The NutraSweet Co. alone has spent $30 million to $40 million per year on advertising, and ads by diet soft drink manufacturers and other companies, who's products carry the swirl trademark of the sugar-free sweetener, would easily send that the figure past $100 million a year.